

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
7 October 2004 (07.10.2004)

PCT

(10) International Publication Number
WO 2004/085478 A3

(51) International Patent Classification⁷: **C07K 19/00 //**
14/47, 14/475, 14/525, 14/52, 14/54, 14/705, 14/715

(21) International Application Number:
PCT/EP2004/003239

(22) International Filing Date: 26 March 2004 (26.03.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
03006949.6 26 March 2003 (26.03.2003) EP

(71) Applicants (for all designated States except US):
APOGENIX BIOTECHNOLOGY AG [DE/DE];
Im Neuenheimer Feld 581, 69120 Heidelberg (DE).
DEUTSCHES KREBSFORSCHUNGSZENTRUM
STIFTUNG DES ÖFFENTLICHEN RECHTS
[DE/DE]; Im Neuenheimer Feld 280, 69120 Heidelberg
(DE).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **WALCZAK, Henning**
[RU/DE]; Keplerstrasse 17, 69120 Heidelberg (DE).

(74) Agents: **WEICKMANN, Franz, Albert et al.**; Weick-
mann & Weickmann, Postfach 860 820, 81635 München
(DE).

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(84) Designated States (unless otherwise indicated, for every
kind of regional protection available): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Euro-
pean (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,
GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK,
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(88) Date of publication of the international search report:
6 January 2005

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: **IMPROVED FC FUSION PROTEINS**

(57) Abstract: The invention relates to fusion proteins comprising at least a first domain and a second domain selected from a
constant Fc immunoglobulin domain.

WO 2004/085478 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/003239

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K19/00
//C07K14/47, C07K14/475, C07K14/525, C07K14/52, C07K14/54, C07K14/705
C07K14/715

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, MEDLINE, EMBASE, WPI Data, PAJ, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 02/079415 A (LEXIGEN PHARM CORP) 10 October 2002 (2002-10-10)</p> <p>page 2, line 12 - line 19 page 3, line 3 - line 10 page 4, line 3 - page 5, line 19 page 6, line 6 - page 7, line 12 page 9, line 28 - page 10, line 3 page 11, line 8 - line 13</p> <p style="text-align: center;">----- --/--</p>	<p>1-4, 9-23, 33-41, 44-46, 51</p>

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *S* document member of the same patent family

Date of the actual completion of the international search

20 September 2004

Date of mailing of the international search report

18. 11. 2004

Name and mailing address of the ISA

European Patent Office, P.B. 5618 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Irion, A

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP2004/003239

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 02/066514 A (MERCK PATENT GMBH ; BAKER MATTHEW (GB); CARTER GRAHAM (GB); HANLON MAR) 29 August 2002 (2002-08-29)</p> <p>page 9, line 30 - line 33 page 10, line 12 - line 23 page 11, line 1 - line 6 page 11, line 13 - line 20 page 12, line 17 - line 19 page 13, line 6 - line 10 page 13, line 28 - page 14, line 22 page 16, line 15 - line 32 page 17, line 12 - line 22 page 18, line 29 - line 31 page 22, line 25 - line 27 page 26, line 10 - line 16 page 28, line 31 - page 29, line 8 page 30, line 4 - line 13</p>	<p>1-4, 9-23, 33-41, 44-46,51</p>
X	<p>SMITH C A ET AL: "CD30 ANTIGEN, A MARKER FOR HODGKIN'S LYMPHOMA, IS A RECEPTOR WHOSE LIGAND DEFINES AN EMERGING FAMILY OF CYTOKINES WITH HOMOLGY TO TNF" CELL, CELL PRESS, CAMBRIDGE, MA, US, vol. 73, 2 July 1993 (1993-07-02), pages 1349-1360, XP002024663 ISSN: 0092-8674 page 1349, right-hand column, paragraph 3 page 1357, left-hand column, paragraph 3</p>	<p>1-4, 9-23, 33-36, 38-40, 44-46,51</p>
X	<p>US 6 015 559 A (LYNCH DAVID H ET AL) 18 January 2000 (2000-01-18) column 16, line 1 - column 18, line 48</p>	<p>5,24,25, 42,43,47</p>
X	<p>WO 95/27735 A (DEBATIN KLAUS MICHAEL ; DEUTSCHES KREBSFORSCH (DE); SCHULZE OSTHOFF KL) 19 October 1995 (1995-10-19) cited in the application page 11, line 13 - page 12, line 14</p>	<p>5,24,25, 42,43,47</p>
X	<p>EP 0 992 243 A (OSAKA BIOSCIENCE INST ; MOCHIDA PHARM CO LTD (JP)) 12 April 2000 (2000-04-12) paragraph '0053! - paragraph '0054! paragraph '0018! - paragraph '0020!</p>	<p>5,24,25, 42,43,47</p>

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/003239

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-5(partially), 9-23 (partially), 24-26 (completely), 33-41(part.)
42-43(compl.), 44-47(part.), 51(part.)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-5 (all partially), 9-23 (all partially), 24-26 (all complete), 33-41 (all partially), 42-43 (all complete), 44-47 (all partially), 51 (partially)

A fusion protein comprising CD95 and a constant immunoglobulin domain, i.e. the sequences as disclosed in Figures 3A and 3B (SEQ ID NO. 15 and 18)

2. claims: 1-5 (all partially), 9-23 (all partially), 27-29 (all complete), 33-41 (all partially), 44-47 (all partially), 51 (partially)

A fusion protein comprising TRAIL-R1, -R2, -R3, -R4 and a constant immunoglobulin domain, i.e. the sequences as disclosed in Figures 5, 7, 8, 10, 12, 13 and 15 (SEQ ID NO. 21-24, 27-32, 34-38, 41-44, 47-52, 54-58, and 61-64).

3. claims: 1-5 (all partially), 9-23 (all partially), 30-32 (all complete), 33-40 (all partially), 44-47 (all partially), 51 (partially)

A fusion protein comprising TNF-R1, -R2 and a constant immunoglobulin domain, i.e. the sequences as disclosed in Figures 17 and 19 (SEQ ID NO. 67-73 and 76-82).

4. claims: 1-5, 9-23, 33-40, 44-46, 51 (all partially)

A fusion protein comprising a VEGF receptor and a constant immunoglobulin domain.

5. claims: 1, 2, 6-23, 33-40, 44, 45, 48, 49, 51 (all partially)

A fusion protein comprising CD95 ligand and a constant immunoglobulin domain.

6. claims: 1, 2, 6-23, 33-40, 44, 45, 48, 49, 51 (all partially)

A fusion protein comprising TRAIL and a constant immunoglobulin domain.

7. claims: 1, 2, 6-23, 33-40, 44, 45, 48, 49, 51 (all partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A fusion protein comprising TNF and a constant immunoglobulin domain.

8. claims: 1, 2, 6-23, 33-40, 44, 45, 48, 49, 51 (all partially)

A fusion protein comprising VEGF and a constant immunoglobulin domain.

9. claims: 1, 2, 6-23, 33-40, 44, 45, 48, 49, 51 (all partially)

A fusion protein comprising IL-15 and a constant immunoglobulin domain.

10. claims: 45 (partially), 50 (complete), 51 (partially)

A fusion protein comprising a biologically active polypeptide and an oligomerising portion of a protein selected from C1q, MBP, SP-1, SP-D, BC, CL43, ACRP30, COMP, and the collagen domain of EDA as disclosed in claim 50.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/003239

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02079415	A	10-10-2002	BR 0208207 A	28-09-2004
			CA 2442363 A1	10-10-2002
			EP 1373301 A2	02-01-2004
			HU 0303753 A2	01-03-2004
			WO 02079415 A2	10-10-2002
			WO 02079232 A2	10-10-2002
			US 2003166877 A1	04-09-2003
WO 02066514	A	29-08-2002	BR 0207267 A	10-02-2004
			CA 2438628 A1	29-08-2002
			WO 02066514 A2	29-08-2002
			EP 1361891 A2	19-11-2003
			HU 0303171 A2	29-12-2003
			US 2004082039 A1	29-04-2004
US 6015559	A	18-01-2000	US 5830469 A	03-11-1998
			US 5620889 A	15-04-1997
			AU 705114 B2	13-05-1999
			AU 7978494 A	04-05-1995
			CA 2174132 A1	20-04-1995
			EP 0723556 A1	31-07-1996
			JP 9503672 T	15-04-1997
			NZ 275711 A	25-03-1998
			WO 9510540 A1	20-04-1995
WO 9527735	A	19-10-1995	AT 255129 T	15-12-2003
			DE 4447484 A1	26-10-1995
			DE 59510836 D1	08-01-2004
			DK 705278 T3	22-03-2004
			WO 9527735 A1	19-10-1995
			EP 1394184 A1	03-03-2004
			EP 0705278 A1	10-04-1996
			ES 2211899 T3	16-07-2004
			JP 8511692 T	10-12-1996
			JP 2004215669 A	05-08-2004
EP 0992243	A	12-04-2000	AT 273713 T	15-09-2004
			AU 4726797 A	22-05-1998
			CA 2270423 A1	07-05-1998
			DE 69730358 D1	23-09-2004
			EP 0992243 A1	12-04-2000
			EP 1449539 A2	25-08-2004
			WO 9818487 A1	07-05-1998
			US 2003109416 A1	12-06-2003